25. The kit according to claim 24, said at least one substance being present as a dry substance, or in a solution, or in the presence of matrix substances.

26. The kit according to claim 25, wherein said matrix substances are salts, buffers, carbohydrates, carboxylic acids, pyrimidines, or inorganic or organic nanoparticles with diameters of up to 1 µm.

REMARKS

The specification is amended, hereby, to reflect the status of the subject application as the national stage of an international application filed under the PCT.

Applicant observes that the Office Action implies, incorrectly, that benefit of priority is sought for the subject application under 35 USC 120.

The specification is further amended, hereby, to delete reference to "Table 1," appearing at page 5 of the specification.

Claims 12-26, presented hereby in place of claims 1-11, are pending.

Claims 12, 16, and 19-26 contain the subject matter of claims 1, 3, and 5-11, amended to address issues raised in the Office Action under §112, ¶2.

Deletion of the reference to "Table 1," hereby, resolves the corresponding objection to the specification contained in the Office Action.

Reconsideration is requested with respect to the rejection of claims under 35 USC 112, ¶2, in view of the changes to the claims effected, hereby, taken in conjunction with the following remarks.

The changes made to claim language by the instant amendment addresses most of the issues raised in the §112, ¶2, statement of rejection.

The statement of rejection under §112, ¶2, includes claim terminology (phrases) allegedly indefinite because "it is not clear what the meets and bounds are for the phrase." These allegations reflect concern with the scope (breadth) of the phrases at issue. As such, the inquiry has no bearing on whether the phrases are indefinite under §112, ¶2, since claim "breadth is not to be equated with indefiniteness." *In re Miller*, 169 USPQ 597, 600 (CCPA 1970). Although an "undoubtedly large number" of embodiments might fall within the scope of a generic expression "the expression is not for that reason indefinite," *In re Skoll*, 187 USPQ 481, 482 (CCPA 1975), and whether a particular embodiment is covered by the expression "is rendered no less certain by the large number." 187 USPQ at 483.

Reconsideration is requested with respect to the rejections of claims 1-11 under 35 USC 112, ¶1, for alleged lack of descriptive support and alleged lack of enablement for embodiments other than the embodiment described in the specification using aminocoumarin-DEVD as the caspase substrate. Reconsideration is requested with respect to the rejection of claim 8 under 35 USC 112, ¶1, for alleged lack of enablement.

According to the statement of rejection for alleged failure to satisfy the written description requirement of §112, ¶1, "one cannot predict the types of additional substrates that can be cleaved by activated caspase in cells undergoing apoptosis." The statement of rejection provides no support, whatsoever, for the allegation. The statement of rejection also alleges that the aforesaid single embodiment using aminocoumarin-DEVD as the caspase substrate does not show possession of the what the rejection terms the "genus of caspase substrate" described and claimed.

The rejection for alleged failure to satisfy the written description requirement under §112, ¶1, is improper because it fails to apply the proper standards for determining compliance with the written description requirement of §112, ¶1. In order to satisfy the requirements of §112, first paragraph, "it is not necessary to embrace in the claims or describe in the specification all possible forms in which the claimed principle may be reduced to practice." *Smith v. Snow*, 294 U.S. 1, 11 (1935). The law does not require an applicant to describe in his specification every conceivable embodiment of the invention. *SRI Int'l v. Matsushita Elec. Corp. of America*, 227 USPQ 577, 586 (Fed. Cir. 1985). "Mention of representative compounds encompassed by generic claim language clearly is not required by §112 or any other provision of the statute." *In re Robins*, 166 USPQ 552, 555 (CCPA 1970). The PTO has the initial burden of providing support for a rejection under §112, ¶1, before the burden shifts to applicant to show the contrary. *In re Bowen*, 181 USPQ 48 (CCPA 1974). Under §112, first paragraph, the concern of the USPTO is support or non-support for a generic term, not its breadth. *In re Marcozzi*, 169 USPQ 367, 369 (CCPA 1971).

The enablement requirement of §112, ¶1, is allegedly not satisfied beyond the scope of the embodiment described in the specification using aminocoumarin-DEVD as the caspase substrate. According to the statement of rejection, it would require undue experimentation to practice the scope of the claims beyond the described embodiment. No evidence, whatsoever, is provided to support the allegation of undue experimentation..

The rejection for alleged failure to satisfy the enablement requirement under §112, ¶1, is improper because it fails to apply the proper standards for determining compliance with the enablement requirement of §112, ¶1. Satisfaction of enablement under 35 U.S.C. 112, first paragraph,

> requires nothing more than objective enablement. . . . [A] specification . . . *must* be taken as complying with . . . 35 U.S.C. 112 *unless* there is reason to do doubt the objective truth of statements relied upon therein.

Staehelin v. Secher, 24 USPQ2d 1513, 1516 (BPA & I 1992) (*emphasis in original*). In order to sustain a rejection for lack of enablement under §112, first paragraph, the PTO must cite evidence in support of any allegations of non-enablement, in addition to explaining *why* it doubts the truth of statements of enablement made in the specification. *In re Sichert*, 196 USPQ 209 (CCPA 1977). Even in an unpredictable area, such as chemistry, the PTO must advance reasons why a patent applicant's broad assertion of enablement is not true. *Bowen, supra.* In order to sustain a rejection for lack of enablement under §112, and shift the burden to a patent applicant, the PTO must advance evidence or reasoning inconsistent with enablement. *Sichert, supra*, Lack of enablement under §112 is not established by mere allegations of undue breadth, that is, by merely arguing that claims read

on non-disclosed embodiments. *Horton v. Stevens*, 7 USPQ2d 1245 (BPA & I 1988). While working examples drawn to specific embodiments may be desirable, they are not *required* in order to satisfy §112. *In re Strahilevitz*, 212 USPQ 561 (CCPA 1982). It is well established that working examples are not necessary, *per se*. *Ex parte Nardi*, 229 USPQ 79 (BPA & I 1986).

Moreover, it would not, in fact, require undue experimentation for the skilled person to extrapolate the invention presently claimed to other caspase detection systems and adapt the method, accordingly, as long as the *cumulated* caspase activity is measured (see further discussion below). It is noted that screening a protein for biological activity is routine, not undue, experimentation. *Ex parte Mark*, 12 USPQ2d 1904 (Bd. Pat. App. & Inter. 1989).

In connection with the §112, ¶1, rejection of claim 8 for alleged lack of enablement, the statement of rejection acknowledges enablement of claim 8 "for screening for possible new chemotherapy." Enablement under § 112 of the statute is, of course, determined from the viewpoint of one of ordinary skill in the art at the time of filing the application for patent, i.e., at the time of constructive reduction to practice. The person of ordinary skill in the art brings with him a knowledge and understanding of the entirety of the prior art up until the date of application.

Since the skilled artisan is well aware of what is already known in the art, providing the same information in a patent specification would be redundant. In "satisfying the enablement requirement, an application need not teach, and preferably omits, that which is well known in the art." *Staehelin v. Secher*, 24 USPQ2d 1513, 1516 (BPA&I 1992). Satisfaction of the enablement requirement does not require the specification to contain a single working example. *Strahilevitz, supra*.

The skilled person knows how to adapt the teachings of the present invention for screening other substances. The skilled person also easily knows how to optimize individual chemotherapy. It is known that patients suffering from cancer diseases may respond differently to certain anti-tumor agents. In order to optimize an individual protocol, a series of experiments can easily be designed by which tumor cells taken from the patient are subjected to treatment with the putative anti-tumor agent. Of course, this can be made in an array, wherein different tumor agents can be applied. The agent that kills the tumor cells will be selected over those that do not kill the tumor cells. Furthermore, an optimization of the dose regime can be performed by measuring the caspase activity due to different concentrations of the putative anti-tumor agent.

Reconsideration is requested with respect to the claim rejections of record under 35 USC 102(b) based on Benjamin and based on Martins.

For anticipation under § 102 to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The absence from a prior art reference of a single claim limitation negates anticipation. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp.* To anticipate the claim, each claim limitation must "*identically* appear" in the reference disclosure. *Gechter v. Davidson*, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997) (*emphasis added*). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

Claim 1 is incorrectly interpreted in the statement of rejection. It ignores, constantly, the important feature (limitation) of the presently claimed invention involving "measuring the *accumulated* caspase activity in the sample" (*emphasis added*). In accordance with the specification (paragraph bridging pages 7 and 8): "It is essential that accumulated caspase activity is measured" (emphasis in original). As this portion of the specification explains, accumulated caspase activity is that which occurs when incubation has lasted long enough to allow for induced apoptosis by all of the substance being tested; and, therefore, "measuring the accumulated caspase activity" as presently claimed requires, inter alia, the measurement to occur only after sufficient incubation time has elapsed for all of the substance tested to induce apoptosis.

Neither Benjamin nor Martins teaches measuring "accumulated" caspase activity, as presently claimed. On the contrary, each of Benjamin and Martins obtained results by using a time-resolved measuring of caspase activity. Therefore, a limitation on the present method claims - "measuring the accumulated caspase activity" - being absent from each of the cited references, anticipation under §102(b) by either reference is negated. *Kolster Speedsteel A B, supra.*

In connection with the "kit" claims, neither cited reference teaches the combination in a *kit* of "a sample support with sample compartments," together with "at least one substance" in each compartment, and further together with "a solution of a reagent standardized for a total number of cells for measuring caspase activity. " As such, limitations on the present claims to a "kit" being absent from each of the cited references, anticipation by either reference is negated. *Kolster Speedsteel A B, supra.*

Reconsideration is requested with respect to the claim rejection of record under 35 USC 102(b) based on an alleged sale or public use of the claimed invention. The rejection cannot be maintained because it fails to show "the invention was . . . in public use or on sale in this country, *more than one year prior* to the date of application for patent in the United States" (*emphasis added*), as required to support a rejection under §102(b).

The subject application was filed in the United States, for purposes of §102(b), on 13 March 2000. 35 USC 363. The §102(b) rejection relies on CLONTECH 2000 Catalogue, page 196, as allegedly describing the presently claimed invention and alleging showing, by implication, a public use or sale thereof. Assuming, arguendo, the aforesaid allegations to be correct, the cited catalogue cannot be relied on to show such public use or sale occurred more than one year before 13 March 2000, the date of filing the subject application in the United States.

On its face, the CLONTECH 2000 Catalogue became available in the year 2000, which of course cannot be more than one year prior to the filing date of an application filed in the United States during that same year. Since the subject application was filed in the United States in the year 2000, the rejection relies on an alleged showing of a sale or public use that, on its face, even if correct did not in fact occur "more than one year prior" to the filing date of the subject application in the United States. Since the alleged sale or public use is not shown to have occurred "more than one year prior" to the filing date of the subject application in the United States, the rejection under §102(b) based on sale or public use of the claimed invention cannot be maintained.

Application No. 09/762,304
Attorney Docket No. P66378US0

Request for Acknowledgment of Foreign Priority Under 35 USC 119

A claim to foreign priority under 35 USC 119 has been made, i.e., in the inventorship declaration, filed April 16, 2001, and the requisite certified copies of the priority documents were filed, and received by the PTO, in accordance with PCT Rules, as evidenced by the Notification of Acceptance, mailed April 30, 2001, by the PTO, and Form PCT/IB304, mailed 12 July 2000 by the International Bureau (a copy of the Form PCT/IB304, mailed 12 July 2000 by the International Bureau, being attached, hereto).

Accordingly, request is made that the Examiner mark the next Office Action to acknowledge, both, the claims to §119 priority and receipt of the certified copies of the priority documents.

Favorable action is requested.

Respectfully submitted,

JACOBSON·HOLMAN PLLC

By: William E. Player
Reg. No. 31,409

400 Seventh Street, N.W.
The Jenifer Building
Washington, D.C. 20004
Tel.: (202) 638-6666
Attorney Docket No. P66378US0
Date: February 19, 2003
WEP/rdt
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Marked up version of amendments

IN THE SPECIFICATION

At page 1, as the first paragraph following the title, add:

This is a 371 of PCT/EP00/02174, filed 13 March 2000.

At page 5, rewrite the third complete paragraph as:

Caspase activity tests are not suitable for the specific detection of apoptosis since necrotic damage, which is not relevant to cytostatic effects, is not covered [(see Table 1)]. The method used in recent years for measuring caspase activity comprise the gel-electrophoretic separation of specific protein substrates as well as chromogenic and fluorogenic tests in which colored products are formed by the caspases (see, e.g., Cohen G.M., Biochem. J. 326: 1-16 (1997), Stennicke H.R., Salvesen G.S., J. Biol. Chem. 41P: 25719-25723 (1997)). All these tests are characterized in that the cells are first sedimented at a particular time after the induction and washed with a buffer, followed by disruption with a lysis buffer for the caspases, which had previously been present in the interior of the cell, to be able to convert the added substrate.

PCT/EP00/02174

AVK | Sg | W | Ca | Hi | NP | ME | TW | JP

25. JULI 2000

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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

To:

- MEYERS, Hans-Wilhelm
Postfach 10 22 41
D-50462 Köln
ALLEMAGNE

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 12 July 2000 (12.07.00)	
Applicant's or agent's file reference 000745woMege	IMPORTANT NOTIFICATION
International application No. PCT/EP00/02174	International filing date (day/month/year) 13 March 2000 (13.03.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 12 March 1999 (12.03.99)
Applicant EVOTEC ANALYTICAL SYSTEMS GMBH et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
12 March 1999 (12.03.99)	199 10 956.7	DE	20 June 2000 (20.06.00)
30 April 1999 (30.04.99)	99108495.5	EP	20 June 2000 (20.06.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
Aino Metcalfe

Telephone No. (41-22) 338.83.38

Form PCT/IB/304 (July 1998)

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